REMARKS

I. Status of the Claims

Claims 1 and 4-13 were pending in the December 3, 2010 Office Action. Claims 4-10 are withdrawn. No claims are amended herewith. Claims 1 and 11-13 are presented for reconsideration.

II. Rejections under 35 U.S.C. § 103

Claims 1 and 11-14 are rejected under 32 U.S.C. 103(a) as being unpatentable over Chen et al. (WO 96/39176) in view of Katz et al. (U.S. Patent No. 4,950,469) and Harley et al. (US 6,641,813).

The Office Action asserts that the cited references render the instant claims obvious because

> Chen et al. teach that oral tolerance to autoantigens can be used to treat antibody mediated autoimmune disease wherein the disease involves antibodies which bind the pertinent autoantigen.... Chen et al. do not teach that the disease provoking antigen is streptococcus which is involved with the pathogenesis of rheumatic fever. Katz et al. teach that rheumatic fever involves an autoimmune antibody response caused by anti streptococcal antibodies which cross react with human tissues.... Katz teaches that agents which prevent binding of said antibodies could be used to treat rheumatic fever.

Office Action at page 3. Applicants request reconsideration and withdrawal of this rejection in light of the following comments.

Chen et al. teach inducing tolerance to autoimmune diseases by oral administration of self autoantigens involved in the disease. However, Chen et al. do not teach or suggest the use of this treatment for any autoimmune disease induced by a pathogen. Additionally, Chen et al. teach only treatment with autologous (self) autoantigens, and not with antigens such as utilized in the process recited in the instant claims, which are not self autoantigens (see below regarding the definition of "autoantigens"), but rather "components or fragments of streptococcus bacteria." Thus, Chen et al. do not teach or suggest the claim element in the instant claims that an

autoimmune disease can be treated by oral administration of a foreign antigen, in this case components or fragments of streptococcus bacteria.

Katz et al. also do not teach or suggest treatment of an autoimmune disease using "components or fragments of streptococcus bacteria," because the induction of autoimmunity by streptococcal proteins was not yet established at the time of filing. Although it was known at the time of filing that a streptococcal infection can induce an autoimmune response, it was not known that exposure to Streptococcus antigens themselves induce the autoimmune response. Thus, the Office Action, at page 4, is incorrect in stating, "...cross reactive bacteria antigens which induce autoimmune antibody responses were already known in the art," since, although it was known that bacterial infections could induce an autoimmune response, the first discovery that bacterial antigens can induce an autoimmune response was made by Quinn et al., 2001, Infect. Immun. 69:4072-4078 (which was a published after the instant application). Quinn et al. states, in the abstract,

> ...we investigated the hypothesis that streptococcal M protein could produce inflammatory valvular heart lesions similar to those seen in rheumatic fever (RF).... The study demonstrates that ... streptococcal M protein can induce an autoimmune cell-mediated immune attack on the heart valve in an animal model. The data support the hypothesis that a bacterial antigen can break immune tolerance in vivo, an important concept in autoimmunity.

Quinn et al. also state, on page 4074, right column, "... our novel observations in the Lewis rat show that streptococcal M protein induced valvular heart disease that strongly resembled valve disease in RF." (emphasis added). Thus, it was clearly unknown at the time of filing that streptococcal antigens could induce autoimmunity. To this point, Katz could not teach that "agents which prevent binding of said antibodies could be used to treat rheumatic fever" as asserted in the Office Action at page 3, since Katz did not have the benefit of that later-published Quinn et al. to establish that streptococcal antigens could induce autoimmunity. Thus, when Katz states, at col. 6, lines 14-16, "[r]heumatic fever is also believed to involve an autoimmune response to streptococcal antigens that are expressed by other tissues, especially cardiac tissues," the skilled

artisan would understand that such a statement is a supposition and not an established fact, since the fact was established by Quinn et al. more than 10 years later.

The Office Action also points to the Chen et al. definition of "autoantigen" at page 8, as including "...antigenic substances that induce conditions having the characteristics of an autoimmune disease when administered to mammals." The full passage from Chen et al. is

> "Autoantigen" **is** any substance or a portion thereof normally found within a mammal that invokes an immune response within an individual.... The term also includes antigenic substances that induce conditions having the characteristics of an autoimmune disease when administered to mammals.

(emphasis added). The above passage would be understood by the skilled artisan as defining an autoantigen as being normally found within a mammal, including antigenic substances that induce conditions having the characteristics of an autoimmune disease when administered to mammals. The passage does not indicate that the "antigenic substances that induce conditions having the characteristics of an autoimmune disease when administered to mammals" is an alternative definition of autoantigen, but rather as describing antigenic substances that are within the definition set forth in the first sentence. As such, the sentence "the term also includes..." would be understood as to be read in the context of the definition of autoantigen in the previous sentence as being normally found within a mammal. Such an interpretation of this passage of Chen et al. is further supported by the fact that nowhere in Chen et al. is it taught or suggested that such an autoantigen could include a foreign antigen. Indeed, the entire teaching of Chen et al. is that administration of the autologous antigenic substance is sufficient to tolerize the mammal to the autoantigen. The skilled artisan would therefore understand from Chen et al. that the above definition of autoantigen would only include autologous (self) antigens. As such, combining Chen et al. with Katz et al. would lead the skilled artisan to use the autoantigen (i.e., the cardiac tissue antigen that is recognized by autoantibodies) to tolerize the mammal as a rheumatic fever treatment, not streptococcal components or fragments as claimed.

Even if the definition of autoantigen in Chen et al. is interpreted to mean an antigen from a pathogen that induces an autoimmune response (a definition to which the Applicant does not subscribe), Chen et al. provides no further discussion or explanation of such embodiments, since Chen et al. only describes the use of autoantigens from the mammal having the autoimmune condition (*i.e.*, self antigens). The skilled artisan would therefore understand that such a passing mention of oral administration of non-self antigens that induce an autoimmune condition is merely a putative suggestion that is not enabled by Chen et al., and would certainly not be considered to be described in Chen et al. sufficiently to satisfy the written description requirement of 35 U.S.C. 112, first paragraph. Thus, the single sentence in Chen et al. that "autoantigen" includes "antigenic substances that induce conditions having the characteristics of an autoimmune disease when administered to mammals" does not establish or even imply that administration of disease antigens from a pathogen that causes an autoimmune disease would be an effective treatment for that disease. Indeed, Chen et al. do not name one disease in this category, nor does Chen et al. even indicate that such antigenic substances could include a disease pathogen. Thus, while the Office Action at page 5 notes that "Chen et al. disclose the use of antigens in humans that are associated with human autoimmune diseases (see page 17-18)," an examination of the table at pages 17-18 of Chen et al. only identify autoantigens that are self antigens. In asserting that such a teaching does provide sufficient written description and enablement for that treatment, the Patent Office thus uses impermissible hindsight by using the teachings of the instant specification to impart written description and enablement to that single sentence in Chen et al. to assert that Chen et al. teaches oral administration of an antigen from a pathogen as a treatment for an autoimmune disease caused by antigens from the pathogen.

The skilled artisan would also understand that Chen et al., alone or in combination with Katz and Harley, do not render the claimed treatment predictable, even though such predictability is required to use the cited combination of references in the instant obviousness rejection (see, *e.g.*, MPEP 2143.01 – "The mere fact that

references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ____, ____, 82 USPQ2d 1385, 1396 (2007)"). Since Katz and Harley do not discuss the use of antigens of pathogens for treatment of an autoimmune disease, those references do not help impart predictability to such treatments.

The Patent Office's assertion that Chen et al. teach treatment of an autoimmune disease by oral administration of an antigen from a pathogen causing the disease also fails to consider that the cited combination of references do not provide a reasonable expectation of success for the claimed treatment, even though such an expectation is required to sustain an obviousness rejection. See, *e.g.*, MPEP 2143.02. Since the only teaching in Chen et al. for that treatment is a single sentence that defines "autoantigen," and since Katz and Harley do not teach or suggest such a treatment, the skilled artisan would understand that the combination of references is insufficient to provide assurance that such a treatment would be effective, since Chen et al. is the only cited reference that is asserted by the Patent Office to provide even a minimal teaching for the oral administration of antigens of a pathogen for treatment of an autoimmune disease caused by that pathogen.

The Office Action further quotes KSR Int'l Co. v. Teleflex, Inc. at page 4 of the Office Action that "if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious...." The Action uses that quote to assert that "Chen et al. teach that oral tolerance to autoantigens can be used to treat antibody mediated autoimmune disease wherein the disease involves antibodies which bind the pertinent autoantigen...." However, the Patent Office is trying to shoehorn the asserted broad definition of autoantigen in Chen et al. to indicate that Chen et al. teaches oral tolerance to both self antigens (which Chen et al. arguably teach) and antigens from a pathogen that causes an autoimmune disease (which Chen et al. do not teach). In so doing, the Patent Office improperly asserts that Chen et al. make obvious the treatment of an

autoimmune disease caused by a pathogen when in fact Chen et al. at most only teach oral tolerance to self antigens.as a treatment for autoimmune diseases. Therefore, a Chen et al. teaching that oral tolerance can be induced to self antigens is not a similar treatment within the meaning of the KSR quote above, such that the skilled artisan would understand that Chen et al. teach nothing about the use of an antigen from a disease organism that causes an autoimmune disease as claimed.

The Action, at page 5, also discusses "...applicants comments about 'artificial antigens' and animal models..." although there was no such discussion in the previous response. Similarly, the discussion about "high dose feeding" on page 6 of the Office Action refers to applicants arguments that were not in the previous response. These comments will not be discussed here since they are irrelevant to the issues at hand.

In light of the above discussion, it is clear that neither Chen et al. nor Katz et al. teach or suggest that an autoimmune disease, in this case rheumatic fever or glomerular nephritis, can be treated with a component or fragment of streptococcus bacteria, as claimed. Since the cited combination of references do not teach or suggest that claim element, the obviousness rejection cannot be sustained. Withdrawal of the rejection under 35 U.S.C. 103(a) is therefore respectfully requested.

III. Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of the rejections of record and passage of all claims to allowance.

The United States Patent and Trademark Office is hereby authorized to charge the extension of time, as well as any other fees required to maintain pendency of this application, to Deposit Account No. 05-1135.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney requests that he be contacted at the number provided below.

Respectfully submitted,

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